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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/774,178	02/01/2001	Tetsuya Ishizuka	P66351US0	7485

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EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/774,178	ISHIZUKA ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/24/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities: The use of the trademark "Gene Amp Thin-Walled Reaction Tubes", page 19, 25) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112 Second paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-9 are vague and confusing because they are drawn to methods, but no clear, active step(s) are recited in the independent claim 1. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion. See *Ex parte Erlich,* 3 USPQ2d, P. 1011 (Bd. Pat. App. Int. 1986). The claims are also confusing because it cannot be determined if the claims are intended to encompass "closed language" such that the RNA is only a specific base sequence or if the claims encompass "open language" or if the claims encompass a "Markush group". Likewise, the claims are overly wordy, especially claims

1 and 8, which makes a clear interpretation of Applicant's intent difficult.

(b) Claims 1 and 8 are confusing at "capable of" because it cannot be determined if the limitations after "capable of" is a property of the template or promoter sequence or whether it is a separate step. Clarification is required.

(c) Claims 3-8 are indefinite and confusing for the addition of parentheses within the claims because it cannot be determined whether the limitation(s) recited in parentheses are intended to be a part of the claimed invention. Clarification is required.

(d) Claim 8 is confusing and indefinite at the recitation of "is characterized in that" because it cannot be determined how the claimed scope is affected. It is suggested that typical U.S. claim language be substituted.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. It is noted that the claims 1 and 8 are extensively wordy, vague and confusing. Therefore, for the purposes of application of prior art, the claim 8 is being interpreted by the Examiner as encompassing multiple generations of double stranded DNA from an RNA template.

6. Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Kievits et al (US 5,654,142, August 5, 1997). Regarding claim 1 and 8, Kievits et al teach a method of

amplifying a target RNA containing a specific base sequence in a sample by an RNA amplification procedure which comprises a step of forming a double-stranded DNA which has a promoter sequence and is capable of transcribing into an RNA comprising a specific base sequence, a step of forming an RNA transcript comprising the specific base sequence using an RNA polymerase and a step of forming a double stranded DNA using the RNA transcript as the template, in the presence of adenosine triphosphate (ATP), guanosine triphosphate (GTP), cytosine triphosphate (CTP), uridine triphosphate (UTP) and inosine triphosphate (ITP) as substrates of the RNA polymerase. Kievits et al also teaches wherein primers complementary to the specific base sequences may be used for multiple generation of double stranded DNA template by the action of a DNA dependent DNA polymerase (col. 3, lines 49 to column 4, line 7; column 5, lines 8- col. 6, lines 29). Therefore, Kievits et al meets the limitations of claims 1 and 8.

7. Claims 1, 6, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakahara et al (Nucleic acids Research, Vol. 26, No. 7, pages 1854-1855, April 1998). Regarding claims 1, 6 and 7, Nakahara et al teach a method of amplifying a target RNA containing a specific base sequence in a sample, the method comprising a step of forming a double stranded DNA which has a promoter sequence and is capable of being transcribed into an RNA comprising the specific base sequence; a step of forming an RNA transcript comprising the bases sequence using an RNA polymerase, wherein said RNA polymerase is a T7 polymerase and a step of forming the double stranded DNA using the RNA transcript as the template in the presence of ATP, UTP, CTP, GTP and ITP and further wherein in the amplification procedure, tris-HCl buffer is present

at a final concentration of 40 mM, Magnesium chloride is present at a final concentration of 12 mM, rNTP are present at a final concentration of 2 mM, and ITP is present at a final concentration of from 0 mM to 4mM (see page 1855, Figure 1 and legend). Nakahara et al additionally teaches wherein the ITP to the other rNTPs encompasses a 1.0:1:0 to a 1.0:1.5 ratio (page 1855, Figure 1 and legend). Therefore, Nakahara et al teach the embodiments of claims 1, 6 and 7 of the instant invention.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 2-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kievets et al and Nakahara et al as previously applied above in view of Brown et al (LabFax, Bios Scientific publishers, Blackwell Scientific Publications, San Diego, California, 1991). Kievets et al Kievits et al teach a method of amplifying a target RNA containing a specific base sequence in a

sample by an RNA amplification procedure which comprises a step of forming a double-stranded DNA which has a promoter sequence and is capable of transcribing into an RNA comprising a specific base sequence, a step of forming an RNA transcript comprising the specific base sequence using an RNA polymerase and a step of forming a double stranded DNA using the RNS transcript as the template, in the presence of adenosine triphosphate (ATP), guanosine triphosphate (GTP), cytosine triphosphate (CTP), uridine triphosphate (UTP) and inosine triphosphate (ITP) as substrates of the RNA polymerase.

Nakahara et al teach a method similar to that of Kievits et al for amplifying a target RNA containing a specific base sequence in a sample, the method comprising a step of forming a double stranded DNA which has a promoter sequence and is capable of being transcribed into an RNA comprising the specific base sequence; a step of forming an RNA transcript comprising the bases sequence using an RNA polymerase, wherein said RNA polymerase is a T7 polymerase and a step of forming the double stranded DNA using the RNA transcript as the template in the presence of ATP, UTP, CTP, GTP and ITP and further wherein in the amplification procedure, tris-HCl buffer is present at a final concentration of 40 mM, Magnesium chloride is present at a final concentration of 12 mM, rNTP are present at a final concentration of 2 mM, and ITP is present at a final concentration of from 0 mM to 4mM (see page 1855, Figure 1 and legend). Nakahara et al additionally teaches wherein the ITP to the other rNTPs encompasses a 1.0:1:0 to a 1.0:1.5 ratio (page 1855, Figure 1 and legend). Kievets et al and Nakahara et al differs from the instant invention in that the references do not teach wherein the RNA polymerase is a Phage SP6 polymerase. Brown provides a general teaching of RNA polymerases and advantages of using them. Brown teaches that the SP6 RNA polymerase is a DNA-dependent RNA

polymerase is highly efficient and is highly specific for the SP6 promoter. Brown teaches that the SP6 polymerase is useful in studies of RNA processing (page 150). Therefore, in view of the foregoing, one of ordinary skill in the art would have been motivated to have modified the method of Kievits et al to encompass a phage SP6 polymerase as the DNA-dependent RNA polymerase in the amplification method instead of the T7 polymerase taught by Nakahara et al for the advantages taught by Brown that the SP6 polymerase is highly efficient and highly specific in studies of RNA processing.

11. Claim 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kievets et al as previously applied above in view Sheldon III et al (US 4,582,789 April 1986). Regarding claims 9 and 10, Kievits et al teach a method of amplifying a target RNA containing a specific base sequence in a sample by an RNA amplification procedure which comprises a step of forming a double-stranded DNA which has a promoter sequence and is capable of transcribing into an RNA comprising a specific base sequence, a step of forming an RNA transcript comprising the specific base sequence using an RNA polymerase and a step of forming a double stranded DNA using the RNA transcript as the template, in the presence of adenosine triphosphate (ATP), guanosine triphosphate (GTP), cytosine triphosphate (CTP), uridine triphosphate (UTP) and inosine triphosphate (ITP) as substrates of the RNA polymerase. Kievets et al further teaches wherein the method may be carried out in the presence of a probe comprising a label (col. 3. line 49 to col. 4, line 14).

Kievets et al differ from the instant invention in that the reference does not teach wherein the probe is labeled with a fluorescent intercalative dye and monitoring the fluorescence intensity

of the reaction solution. The reference also does not teach wherein the fluorescent intercalative dye alters its fluorescence upon hybridization with the RNA transcript. Sheldon III et al provides a general teaching of labeling nucleic acids, preferably probes, with an intercalation moiety (dye) capable of altering its fluorescence property for use in hybridization assay for detecting nucleic acids (col. 6, lines 5-27, lines 43-68; col. 17, lines 3-41; col. 20, lines 33-50). Sheldon III et al teach that the labeled probed comprising an intercalative moiety is useful in application for detecting nucleic acid sequences (RNA/ and or DNA) such as e.g., those characteristic of a pathogenic microbe or those responsible for or linked to a genetic disease (col. 17, lines 3-7). Therefore, in view of the foregoing, one of ordinary skill in the art would have been motivated to have encompassed an intercalative moiety to the probe as taught by Kievets et al for the advantages of detecting nucleic acid sequence (RNA sequences) characteristics responsible for or linked to a genetic disease as suggested by Sheldon III et al.

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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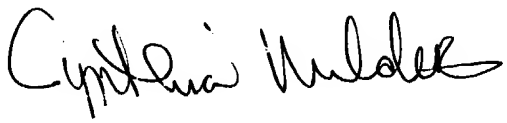

CYNTHIA WILDER
PATENT EXAMINER

9/18/2004